

(b) providing a second mammalian cell line which produces the enzyme at a lower level than the first cell line, or does not produce the enzyme at all, and which exhibits said phenotypic response to the enzyme to a lesser degree or not at all;

(c) incubating the chemical agent with the first and second cell lines; and

(d) comparing the phenotypic response of the first cell line to the chemical agent with the phenotypic response of the second cell line to the chemical agent.

²² 34. The method of Claim ¹¹ 33 wherein said first cell line is obtained by introducing a gene encoding said enzyme into a host cell, said gene being under the control of a promoter functional in the host cell, whereby said gene is expressed.

35. The method of Claim 34 wherein the gene is introduced into the host cell by means of a first genetic vector into which the gene has been inserted, and said second cell line is obtained by introducing into a similar host cell a second genetic vector essentially identical to the first genetic vector except that it does not bear said gene insert.

³ 36. The method of ^{either Claim 33 or Claim 34} ~~any one of Claims 33-35~~ wherein said chemical agent is a suspected inhibitor of the biological activity of said enzyme.

⁴ 37. The method of ^{either Claim 33 or Claim 34} ~~any one of Claims 33-35~~ wherein said chemical agent is a suspected activator of the biological activity of said enzyme.

^C 38. The method of ^{Claim 34} ~~any one of Claims 33-35~~ wherein the phenotypic response of said first cell line upon incubation with said chemical agent is a graded cellular response.

39. A method of determining whether a chemical agent that directly interacts with a protein is an inhibitor or activator of that protein whose production by a cell evokes a responsive change in a phenotypic characteristic of the cell, other than the level of said protein in said cell per se, which comprises:

(a) providing a first mammalian cell line which produces said protein and exhibits said phenotypic response to the biological activity of the protein;

(b) providing a second mammalian cell line which produces the protein at a lower level than the first cell line, or does not produce the protein at all, and which exhibits said phenotypic response to the biological activity of said protein to a lesser degree or not at all;

(c) incubating the chemical agent with the first and second cell lines, wherein said chemical agent is suspected of being an inhibitor or activator of the biological activity of the protein; and

(d) comparing the phenotypic response of the first cell line to the chemical agent with the phenotypic response of the second cell line to the chemical agent.

40. The method of Claim 39 wherein said first cell line is obtained by introducing a gene encoding said protein into a host cell, said gene being under the control of a promoter functional in the host cell, whereby said gene is expressed.

41. The method of Claim 40 wherein the gene is introduced into the host cell by means of a first genetic vector into which the gene has been inserted, and said second cell line is obtained by introducing into a similar host cell a second genetic vector essentially identical to the first genetic vector except that it does not bear said gene insert.

42. The method of ^{Claim 40} ~~any one of Claims 39-41~~ wherein the phenotypic response of said first cell line upon incubation with said chemical agent is a graded cellular response.

43. A method of determining whether a chemical agent that directly interacts with an enzyme is an inhibitor or activator of that enzyme which comprises:

(a) providing a mammalian test cell which overproduces a selected enzyme relative to a mammalian control cell which produces said enzyme at a lower level or essentially does not produce the enzyme, and wherein production of said enzyme in said test cell evokes a

RECEIVED
JUL 14 2000
TECH CENTER 1600/2900

70

B

responsive change in a phenotypic characteristic of said test cell, other than the level of said enzyme in said test cell per se, which is comparatively greater than in said control cell;

(b) treating said test cell containing the overproduced selected enzyme with said chemical agent; and

(c) examining the treated test cell to determine whether it exhibits a change in said phenotypic characteristic in response to said chemical agent.

⁴⁶
~~44~~. The method of Claim ~~43~~⁵⁵ wherein said test cell is obtained by introducing a gene encoding said enzyme into a host cell, said gene being under the control of a promoter functional in the host cell, whereby said gene is expressed.

⁷⁷
~~45~~. The method of Claim ~~44~~⁶⁶ wherein the gene is introduced into said host cell by means of a first genetic vector into which the gene has been inserted, and said control cell is obtained by introducing into a similar host cell a second genetic vector essentially identical to the first genetic vector except that it does not bear said gene insert.

⁸
~~46~~. The method of Claim ~~45~~⁵⁵ wherein examination for a change in the phenotypic characteristic in response to said chemical agent includes comparing the response of the treated cell to the response of a comparable untreated test cell.

⁹
~~47~~. The method of Claim ~~46~~⁵⁵ wherein examination includes comparing the phenotypic response of the treated test cell to that of a comparably treated test cell which does not overproduce the selected enzyme.

¹⁰
~~48~~. The method of Claim ~~47~~⁵ wherein examination includes comparing the phenotypic response of the ~~first~~ test cell in the presence of said chemical agent with the phenotypic response of ^athe second test cell in the presence of a known inhibitor or activator of the enzyme.

⁵⁻¹⁰
49. The method of any one of Claims ~~43-48~~ wherein said chemical agent is a suspected inhibitor of the biological activity of said enzyme.

⁵⁻¹⁰
50. The method of any one of Claims ~~43-48~~ wherein said chemical agent is a suspected activator of the biological activity of said enzyme.

51. The method of any one of Claims ~~43-48~~ wherein said change in said phenotypic characteristic in response to said chemical agent is a graded cellular response.

52. A method of determining whether a chemical agent that directly interacts with a protein is an inhibitor or activator of that protein which comprises:

(a) providing a mammalian test cell which overproduces a selected protein relative to a mammalian control cell which produces said protein at a lower level or essentially does not produce the protein, and wherein production of said protein in said test cell evokes a responsive change in a phenotypic characteristic of said test cell, other than the level of said protein in said test cell per se, which is comparatively greater than in said control cell;

(b) treating said test cell containing the overproduced selected protein with said chemical agent, wherein said chemical agent is suspected of being an inhibitor or activator of the biological activity of said protein; and

(c) examining the treated test cell to determine whether it exhibits a change in said phenotypic characteristic in response to said chemical agent.

53. The method of Claim 52 wherein said test cell is obtained by introducing a gene encoding said protein into a host cell, said gene being under the control of a promoter functional in the host cell, whereby said gene is expressed.

54. The method of Claim 53 wherein the gene is introduced into said host cell by means of a first genetic vector into which the gene has been inserted, and said control cell is